Amendments to the Specification

Please replace the title with the following <u>new</u> title:

<u>Human Myosin-Like Polypeptide Expressed Predominantly in Heart and Muscle</u>

Please replace the paragraph on page 1 lines 4-17, with the following amended paragraph:

<u>This application is a divisional application of U.S. patent application number 09/866,108 filed May 25, 2001, the entire disclosure of which is hereby incorporated by reference.</u> This application claims priority under 35 U.S.C. § 119(e) to provisional applications for United States Patent nos. 60/207,456, filed May 26, 2000, 60/234,687, filed September 21, 2000, 60/236,359, filed September 27, 2000, and 60/266,860, filed February 5, 2001, claims priority under 35 U.S.C. § 365(c) to international application nos. PCT/US01/00666, PCT/US01/00667, PCT/US01/00664, PCT/US01/00669, PCT/US01/00665, PCT/US01/00668, PCT/US01/00663, PCT/US01/00662, PCT/US01/00661, PCT/US01/00670, all filed January 30, 2001, and claims priority under 35 U.S.C. § 119(a) to GB 0024263.6, filed October 4, 2000, the disclosures of which are incorporated herein by reference in their entireties.

Please replace the paragraph on page 2 lines 3-9, with the following amended paragraph:

The present application includes a Sequence Listing filed herewith on ~~a single (CD-R) compact~~<u>one (1) CD-R</u> disc, provided in duplicate. ~~The Sequence Listing is presented in,~~<u>containing</u> a single file named ~~sequence~~<u>PB0105DIV Sequence Listing</u>.txt,

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~~last modified 05/24/01 02:36p, and~~ having ~~2,283,433 bytes~~2,259 kilobytes, last modified November 25, 2003, and recorded November 25, 2003. ~~the disclosure of which~~The Sequence Listing contained in said file on said disc is incorporated herein by reference in its entirety.

Please replace the three paragraphs on page 15 lines 3-12, with the following amended paragraphs:

FIGS. 2A – 2L collectively show the sequence of the cDNA encoding the human genome-derived myosin-like protein (hGDMLP-1) of the present invention (full-length cDNA (bases 1 – 8117) = SEQ ID NO:1; coding sequence (bases 170 – 7876) = SEQ ID NO:2), with its predicted amino acid sequence (SEQ ID NO:3);

FIGS. 3A – 3C collectively show an alignment of residues 505 – 2249 of the hGDMLP-1 coding sequence of the present invention (SEQ ID NO:3) with the two closest known orthologues (BAA93660 = SEQ ID NO:15753; BAA13206 = SEQ ID NO:15754);

FIG. 4 shows an alignment of residues 1802 – 1907 of the amino acid sequence of hGDMLP-1 of the present invention (SEQ ID NO:3) and residues 82 – 180 of human myocilin (SEQ ID NO:15755);

Please replace the paragraph on page 29 lines 23-32, with the following amended paragraph:

Accordingly, the hGDMLP-1 cDNA clone described herein has been deposited in a public repository (American Type Culture Collection, Manassas, Virginia, USA). The

deposit, <u>made according to the Budapest Treat on the International Recognition of the</u> <u>Deposit of Microorganisms for the Purposes of Patent Procedure, was</u> received at ATCC on May 23, 2001, ~~has been accorded an accession date after viability testing of~~ ~~_____ and accession number of _____~~ <u>and given an accession number of</u> <u>PTA-3397</u>. Any errors in sequence reported herein can be determined and corrected by sequencing nucleic acids propagated from the deposited clones using standard techniques.

Please replace the paragraph on page 30 line 31 through page 31 line 12, with the following amended paragraph:

For purposes herein, percent identity of two nucleic acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at <u>the at the National Center for Biotechnology Information (NCBI) website.</u> ~~_____ http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html.~~ To assess percent identity of nucleic acids, the BLASTN module of BLAST 2 SEQUENCES is used with default values of (i) reward for a match: 1; (ii) penalty for a mismatch: -2; (iii) open gap 5 and extension gap 2 penalties; (iv) gap X_dropoff 50 expect 10 word size 11 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 82 line 28 through page 83 line 3, with the following amended paragraph:

Bacterial cells can be rendered electrocompetent — that is, competent to take up exogenous DNA by electroporation — by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided online in <u>Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735,</u> BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~.

Please replace the paragraph on page 84 lines 10-31, with the following amended paragraph:

For chemical transfection, DNA can be coprecipitated with $CaPO_4$ or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for $CaPO_4$ transfection (CalPhos™ Mammalian Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER, (Roche Molecular Biochemicals, Indianapolis, IN USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA). Protocols for electroporating mammalian cells can be found online in <u>Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735,</u> BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~. See also, Norton et al. (eds.), <u>Gene</u>

Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000) (ISBN 1-881299-34-1), incorporated herein by reference in its entirety.

Please replace the paragraph on page 86 line 21 through page 87 line 4, with the following amended paragraph:

For purposes herein, percent identity of two amino acid sequences is determined using the procedure of Tatiana et al., "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at the National Center for Biotechnology Information (NCBI) website.
~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html,~~
To assess percent identity of amino acid sequences, the BLASTP module of BLAST 2 SEQUENCES is used with default values of (i) BLOSUM62 matrix, Henikoff et al., *Proc. Natl. Acad. Sci USA* 89(22):10915-9 (1992); (ii) open gap 11 and extension gap 1 penalties; and (iii) gap x_dropoff 50 expect 10 word size 3 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 152 lines 13-23, with the following amended paragraph:

Motif searches using Pfam (Washington University, St. Louis, web site~~http://pfam.wustl.edu/~~), SMART (European Molecular Biology Laboratory, Heidelberg, web site~~http://smart.embl-heidelberg.de/~~), and PROSITE pattern and profile

databases (<u>Expert Protein Analysis System (ExPASy) website</u>

~~http://www.expasy.ch/prosite/~~), identified several known domains. A myosin head (also

denominated myosin motor, large ATPase) domain is encoded by amino acid residues

566 - 1335; a myosin tail domain is located at residues 1422 - 1919. Given the presence

of a myosin head and a myosin tail, we have denominated the gene "human genome-

derived myosin-like protein-1" ("hGDMLP-1").

Please replace the paragraph on page 164 lines 13-24, with the following amended

paragraph:

Using PROSCAN, <u>available at the National Institutes of Health web site</u>

~~(http://bimas.dcrt.nih.gov/molbio/proscan/)~~, no significant promoter was identified in the

putative promoter region. However, transcription factor binding sites were identified

using <u>MOTIF, available at the GenomeNet web site (Bioinformatics Center, Institute for</u>

<u>Chemical Research, Kyoto University)</u>~~a web site at http://motif.genome.ad.jp/~~, including

a SRY (sex-determining region Y gene product) binding sites (134..140 bp, with

numbering according to SEQ ID NO:15,752), and a couple of MZF1 (myeloid zinc finger

1, a negative regulator of CD34 and c-myb, and responsive to retinoic acid) binding sites

(1843..1850 bp and 403-395 bp).